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# ON LESIONS OF THE MID-BRAIN, WITH SPECIAL REFERENCE TO THE BENEDICT SYNDROME.

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Direct experiment upon the structures of the central nervous system of man is necessarily limited, and the results of such experimentation upon lower animals, even those nearest to man, leave much to be desired from the standpoint of interpretation.

Disease, however, is a ruthless experimenter. Its technique knows no refinements, and when its field of operation involves the central nervous system the natural reparative processes do little to overcome the blunders of its workings. Hence the persistence of the defects, and the exasperating struggles in the attempts at therapeutic relief.

There are compensations, however, for the permanencies of disease of these structures make possible definite contributions to nervous physiology and anatomy, which are largely denied by the experimental path, although this latter mode of approach, as carried on in lower animals, rounds out the pictures offered by nature's experimenter, disease.

The mid-brain offers an especially attractive field in this respect, and notwithstanding the complications of its structure, we are in a position to-day to read more clearly the clinical pictures that affections of this portion of the nervous system may produce.

The mid-brain is one of the smallest divisions of the central nervous system, yet within it are situated most of the neural mechanisms essential to proper functions. It contains nearly all of the incoming sensory tracts, important stations in the cerebellar paths, the entire group of motor conducting fibres, certain nuclear structures of the sympathetic nervous system, and some nuclei of the cranial nerves. By reason of the compactness of its anatomical arrangements, its lesions are apt to be accompanied by many clinical signs, which offer a series of classical groupings. These groupings offer much suggestive material bearing on topographical diagnosis, and for this purpose lesions in the mid-brain are particularly illuminating.

The longitudinal section of the brain stem shows the limitation of this area, bounded caudad by the forward edge of the pons and cephalad by the upper border of the anterior corpora quadrigemina. The aqueduct of Sylvius penetrates its entire length in its dorsal aspect. On cross section a division into three fairly well demarcated areas is apparent: the cerebral peduncles below, divided by the substantia nigra into the base and the tegmentum, and the anterior and posterior corpora quadrigemina above. It contains two large paired structures, the red nuclei. Its chief nuclear structures then are the anterior and posterior corpora quadrigemina, the red nuclei, the nuclei of the third and fourth nerves, the central grey neuclei, the small nuclei of the fifth nerve, the nuclei of the posterior commissure and of the posterior longitudinal bundles, and the substantia nigra. At its upper border it is in close relation to the thalamus, and the median and lateral geniculate bodies, while smaller nuclear masses as yet little known are the dorsal and deep tegmental nuclei and the interpeduncular ganglia of Gudden.

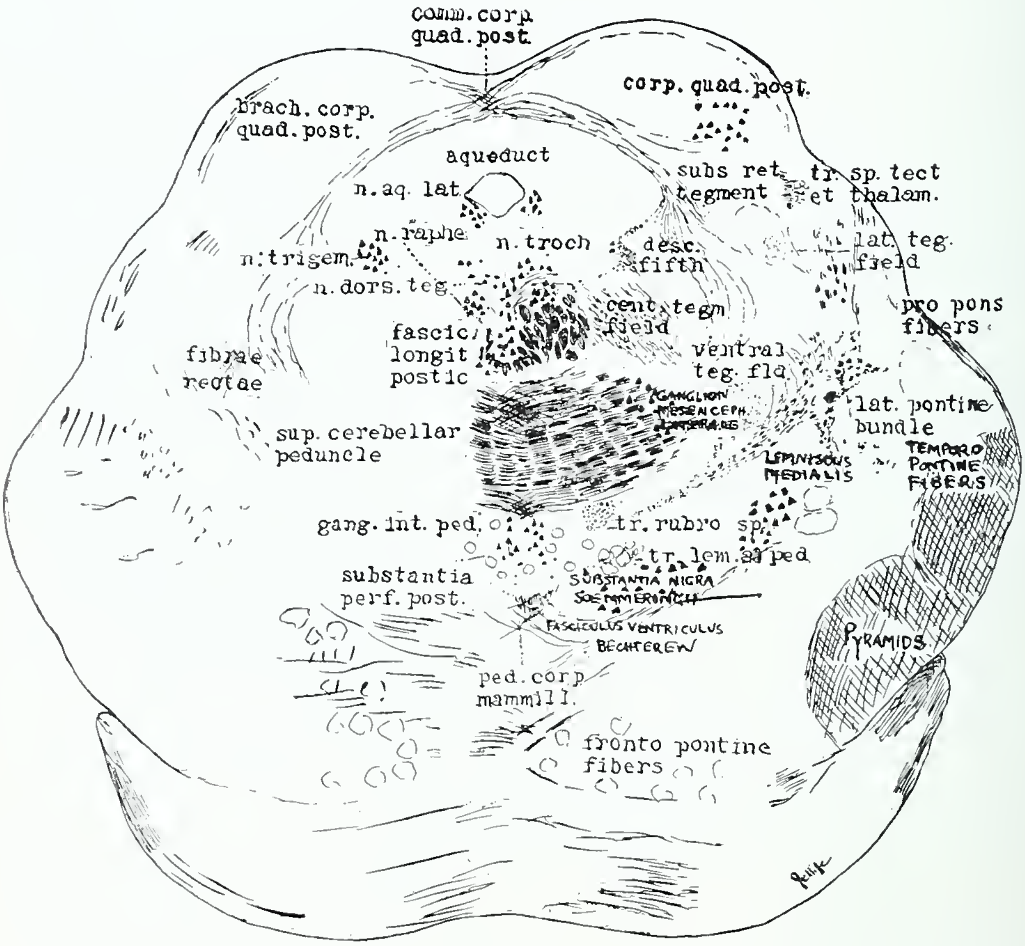

Fig. 1. Section of mid-brain at lower level about crossing of superior cerebellar peduncles. (Original.)

The chief anatomical features may be seen in the accompanying cross sections, which represent the sections taken respectively at the pontine end, the middle, and the upper end of the mid-brain.

Four characteristic syndromes are described for lesions in this region. These represent only the more striking of the many pictures due to lesion in this area. They are the Weber (Gruebler-Weber) syndrome, the syndrome of Benedict, as Charcot names it, the Nothnagel syndrome, as Marburg suggests, and the syndrome of Combe.

The Weber (Gruebler-Weber) syndrome consists of a hemiplegia of one side with oculomotor palsy of the other side. It is one of the commonest of the symptom-groupings of mid-brain disease, and is due either to a lesion of the base, compressing one peduncle at about the point of egress of the oculomotor nerves, or to a lesion within the substance of the cerebral peduncles. The site of the lesion may be seen in the accompanying sketches, which show the areas involved—for instance in a thrombosis of the posterior cerebral artery—arteria profunda cerebri. (Gruenewald: Zur Kenntniss der Thrombose der Arteria profunda Cerebri, *Deutsche Zeitschr. fuer Nervenheilk,* 41, p. 485, 1911; and in a case reported by Cestan, *Revue Neurologique,* 1901. See Figs. 4-5.)

The present communication takes up the second of the mid-brain syndromes—namely, that of Benedict. This consists of a Weber syndrome plus a tremor on the side of the hemiplegia; that is some oculomotor palsy, with crossed hemiplegia, and movements usually of the nature of a cross between a paralysis agitans and a multiple sclerosis: a persistent tremor, which increases on motion to a slight extent.

Benedict described this condition in the first edition (1872) of his "Nervenpathologie." He spoke of it as a symptomatic chorea. In his second edition (1874, p. 253) he said "In the first edition of my book, I have expressly stated that following an acute cerebritis in children, a hemichorea can persist, and as a matter of fact this occurs with the definite symptom complex of an acute cerebritis after an exanthematous disease. I have already separated these cases as symptomatic choreas. They constitute chronic affections, and are usually associated with hemiparesis."

I have never seen his original case quoted, so give it here briefly (from his second edition, 1874, p. 311, obs. 214), as his first edition is not available. It is put under the caption "Paralysis Agitans" in the second edition: "V. Feld, four years old, admitted May 29th, 1872. Six months ago was sick with marked headache for four weeks. He had right ptosis at this time, and now has a right oculo-motor palsy and left abducens palsy. The head is sunk against the left shoulder, but could be held upright. The chin points to the right. There are tremors of the left hand. The patient can walk, but not far. The leg is over-extended at the knee, and is in constant motion. Upon executing certain movements, tremor is developed. There is no atrophy, no convulsions, no unconsciousness, no neuroretinitis.

"Next month the patient had a convulsive attack, with loss of consciousness. There was marked dyspnea. Two days later, another similar attack, which lasted half an hour. Following this convulsive seizure, the patient staggered like a drunken man. Nine days later the patient had another seizure, and was unconscious half a day. He died a month later.

"Autopsy showed tubercles in the frontal lobe, in marginal gyri and in central convolutions; one in the cingulum. A tubercle the size of a pigeon's egg in the right peduncle, extending forward to the posterior perforated lamina. It involved the optic tract, and destroyed the right oculo-motor fibres. The left cerebellar peduncle was pushed to the left. There was involvement of the third ventricle and the right colliculus was pressed upon and partly destroyed."

In 1888 (*Mitth. d. Wien. med. Doct. Coll.*, p. 230) Benedict presented an adult with the syndrome, remarking upon the individuality of the disorder—which he says consists of an oculo-motor palsy of one side, combined with a hemiplegia of the opposite side and a tremor in the paralyzed extremity. In the patient presented the oculo-motor palsy took place three years previously, the left sided hemiplegia and tremor gradually. The tremor has some of the features of a multiple sclerosis tremor in that it is increased on intentional movement.

It may be seen from this short summary that the character of the tremor was somewhat puzzling to Benedict, in that he allied it successively with chorea, with paralysis agitans, and with multiple sclerosis. This uncertainty has not been confined to Benedict, however, for tremors due to mid-brain lesions are of a very diverse nature, as has been well shown by Holmes* and Marburg,** and as I have attempted to bring out in a paper recently read before the American Neurological Association,*** where the whole subject is discussed somewhat at length.

Before going on further, I desire to present the history of a patient, showing the history of the Benedict syndrome, which has however partly cleared up, leaving the tremor and some hemianopsia. Case I.—A. K., aged thirty-two, born in Austria. Her family history shows tuberculosis of the father, who died when she was very young. There were nine children in the family, five alive and well, four died in infancy. Hereditary factors unknown.

Patient was normally born, no eruptions, and learned to walk and talk at the proper time. Read at the age of six. At the age of seven had scarlet fever, was sick three months, and had a meningitic attack of uncertain character which left her very feeble, and an invalid for a year, but she had no paralysis, and no history of any tremor. She had no childish neuropathic signs, did not wet her bed at night, nor have bad dreams. She attended school until the age of fourteen, began to menstruate at seventeen, had had no adult diseases, no history of syphilis, no eruptions or scars. She has never had any convulsions, nor fainting attacks, and beyond an attack of cellulitis and headaches has always con-

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*Holmes (*Brain*, 1904).

***Wien. klin. Wochenschr.*, 1905.

***Jelliffe: On Some Obscure Tremors Due to Mid-Brain Lesions.

sidered herself healthy. The death of her first husband, and the desertion of her second were her only emotional shocks. Nothing suggestive of a hysterical temperament save an incomplete account of two attacks of color blindness.

About two years ago she had a uterine operation, following severe headaches, but made a good recovery, and was fairly well until May 15th, 1910. Her husband was still living with her, and there was no intimation, she says, of any impending domestic difficulties.

Two weeks previously to May 15th, 1910, she had had severe headaches. One morning while collecting rents for the janitor, she suddenly collapsed and was semiconscious for a few moments. She then found that she could hardly walk because of the weakness of the right leg, and that it grew numb, and she lost all feeling in it. She went to bed, and while there the whole right side felt heavy and numb. She was dull and indifferent for several days, and could not feel the right side of her body as formerly. She noted that her right nostril seemed to be plugged up, and that she could not see as clearly as before. She had some difficulty with the left (?) eyelid. The right side of the face and lips, and inside of the mouth appeared less sensitive. No pain. She said her speech was at first slightly indistinct; she stuttered, and could not move the right side of her face. She had no tendency to cry nor to weep. She saw double she thought but was not positive. The headache cleared up rather suddenly.

She was in bed two weeks, and then began to improve, at first being stiff in walking. The sensibility returned in her right side, her speech improved, and became normal she thinks within three months. The sight cleared up after two weeks. (She still has a hemianopsia unknown to her.)

For the past three weeks she has been having some prickling pains in the right arm, and also in the face, but they are not severe. The right hand has perspired more than the left. For two months past says she cannot work as a waitress, as she cannot hold the tray with her right hand, it commenced to tremble, and now she drops things from it. She says she cannot remember things as well as formerly.

Patient was seen October 15th, 1910.

*Status Nervorum.*—No cranial abnormalities. No painful percussion noted over head.

Smell is normal on each side.

Sight is apparently normal according to patient.

Examination for hemianopsia reveals marked homonymous hemianopsia, and retraction of fields. Wernicke's hemianopic pupillary phenomenon doubtfully present.

There are no scotomata and the fundi are apparently normal. Eye movements normal in all directions. There is slightly nystagmoid twitching on looking to the side. No diplopia.

Pupils are medium to small—3 to 4 mm.—round, equal in size; all

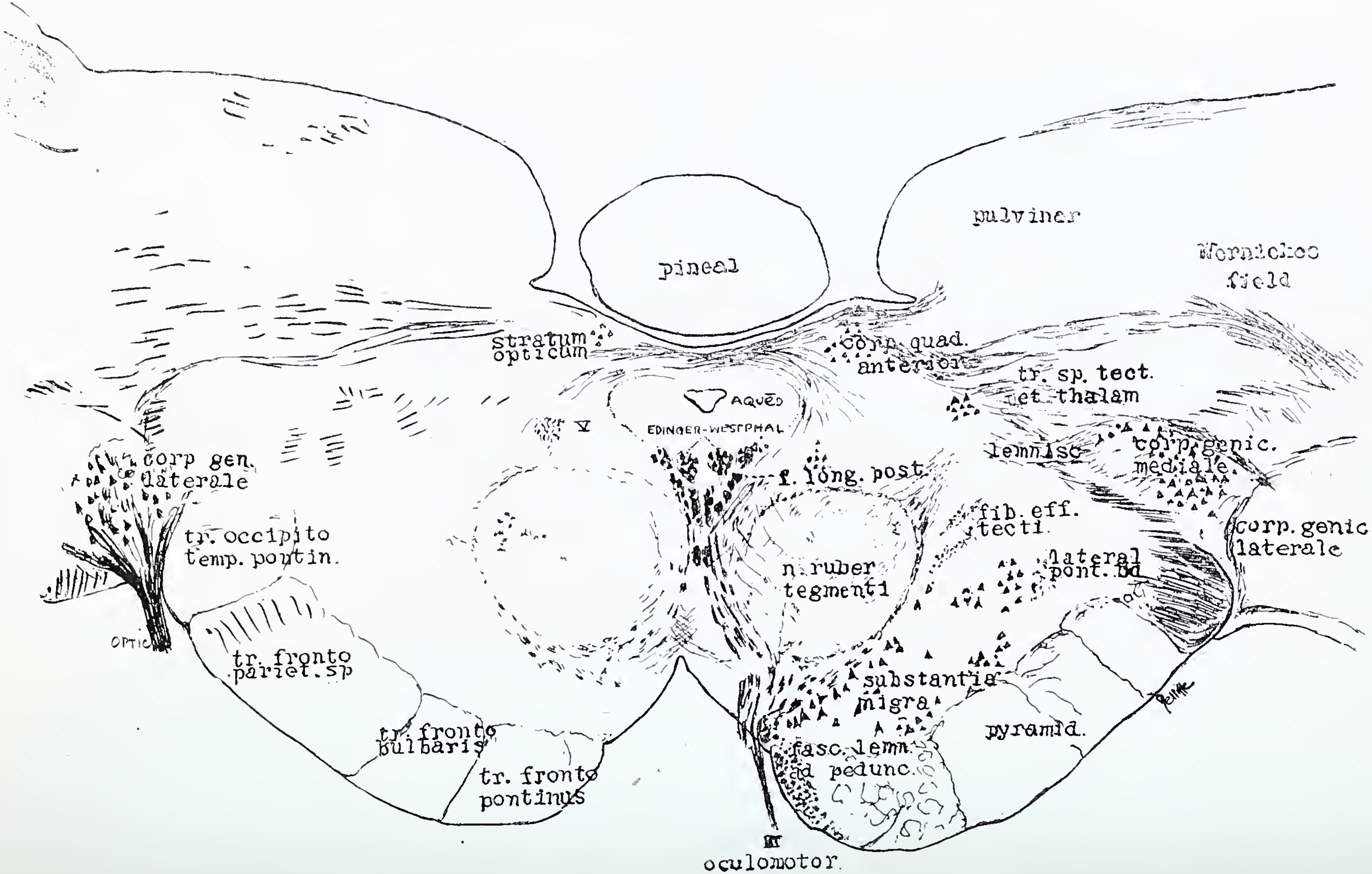

Fig. 2. Section of mid-brain at about middle. (Original.)

reflexes, light, direct and consensual, convergence, accommodation **and** sympathetic active and ample.

The trigeminal functions, motor and sensory are intact.

The facial innervation is symmetrical, and no trace of former possible ptosis. Hearing is slightly impaired on the right side. Rinné and Weber are normal. Vestibular function—galvanic and caloric—normal.

Facial reflexes normal, soft palate slightly to right side, tongue protrudes slightly to right. Speech is normal with slight hesitancy at times. Test phrases well pronounced. No sensory aphasia disturbance, no agraphia and no apraxia.

Upper extremities show no atrophies, hypertrophies, spasms nor hypotonus. Muscular power good, equal on two sides. Nerve trunks are not tender. Reflexes present and equal on both sides.

There is a very distinct tremor of the right hand, which is best described as a hybrid of a paralysis agitans and an intention tremor. Left hand intact.

She has no astereognosis, slight clumsiness of right hand, left very deft. Sensibility to all forms of stimulation apparently intact. Slightly increased moisture of right hand and arm pits.

*Trunk.*—Power normal. No painful points along spine; no unilateral pressure points over mammary or ovarian regions. Sensibility intact; motor power intact; no marked dermographia; abdominal reflexes O. K.

*Lower Extremities.*—No atrophies, hypertrophies, spasms, nor hypotonus. Muscular power good and equal. Knee jerks equal; Achilles right slightly greater than left. No clonus, no Babinski nor Oppenheim, no painful nerve trunks, no Lasègue. Gait normal forward and backward, with open and closed eyes; no dizziness with different head positions, sensibility intact. No asynergia, and no vasomotor or trophic disturbances.

*Status Corporis.*—Normal, with question as to slight heart murmur.

*Summary.*—An apparently healthy woman of thirty-two, with possible mild heart lesion following severe scarlet fever at age of seven, suddenly develops with semiunconsciousness a mild right-sided hemiplegia, with hemianesthesia, hemianopsia and speech disturbance, and crossed (?) oculomotor signs. She makes a rapid recovery, and after three months commences to develop a tremor of the right arm. After five months, then in apparent good health, she has a residual homonymous hemianopsia of the right side, a right-sided tremor resembling that of paralysis agitans, with slight intention quality, and only traces of her former hemiplegia—tongue to right—increased Achilles in right side.

Before discussing the implications of this case, a brief glance may be taken at the post-hemiplegic motor disturbances with which the case is allied, and which have been very extensively treated of in the literature, but which notwithstanding are not definitely located.

It will be recalled that Kahler and Pick believed that these post-

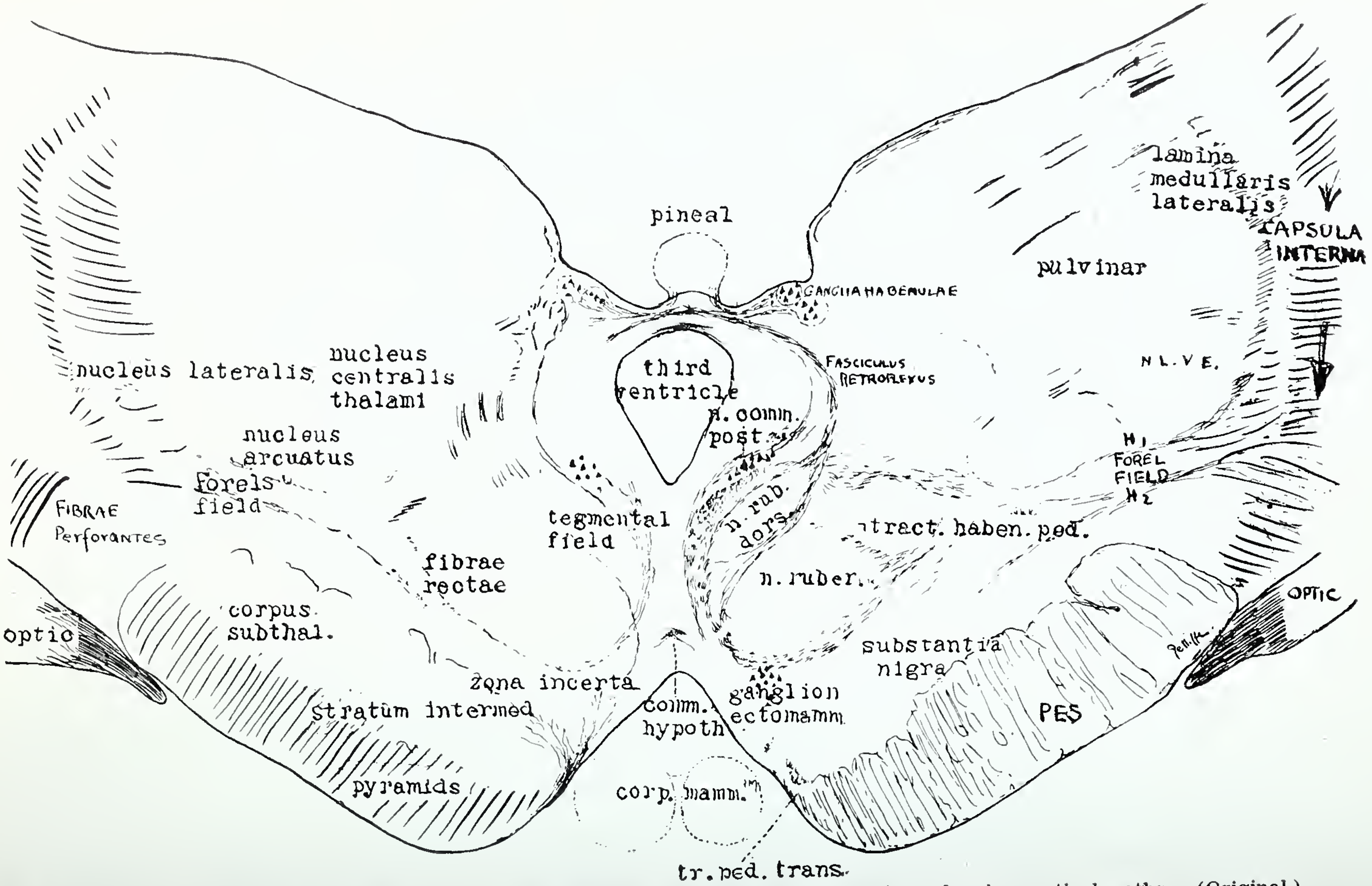

Fig. 3. Upper end of mid-brain; anterior end of red nucleus, showing rubro-thalamic and rubro-cortical paths. (Original.)

hemiplegic motor disturbances were due to some involvement of the pyramidal system. Charcot later constructed a special path in the internal capsule which, being involved, he thought caused a hemi chorea.

Bonhœffer attacked the problem in1901, and placed the lesion for these motor disturbances in the superior cerebellar peduncle system. It has already been pointed out that the chief station of this system is in the mid-brain, and that it centers about the red nucleus. This structure receives the involuntary tonic innervating fibres from the cerebellum from the spinal side; sends fibres to the thalamus—rubro thalamic fibres, and also sends and receives fibres from the cortex by way of the lenticular nucleus and through other paths not yet completely worked out. (See v. Monakow: Der Rote Kern, 1910.) Caudally the rubro-spinal tract descends to join the pyramidal tract and constitutes the chief tonic reflex path, conveying both cerebello-rubro spinal impulses, and cortico-rubro-bulbo-spinal impulses.

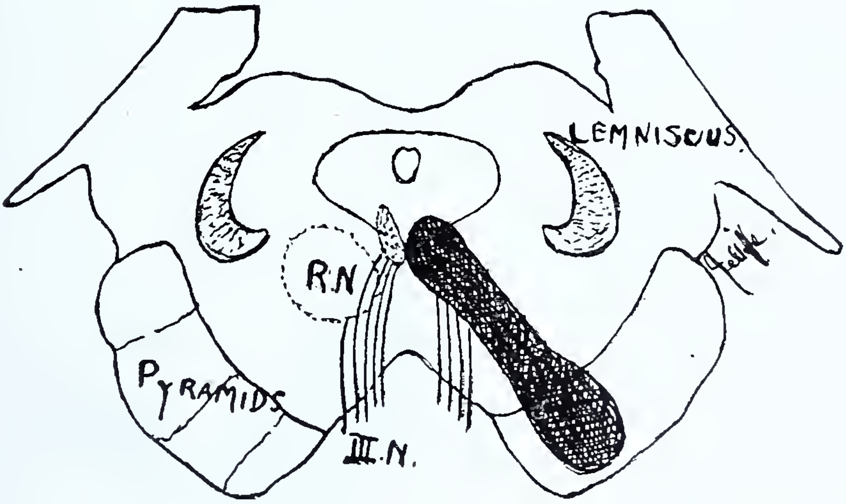

Fig. 4. Gruenewald's case of Weber syndrome. Location of degeneration in black.

In view of the complexity of these connections the difficulty of accurate localization of these post hemiplegic movements becomes apparent.

A glance at the reported cases shows a variety of movements.* Thus there is simple tremor in the cases of Pilz, Fleischmann, Bristowe, Hoppe, Bonaforte, and Raviard. In the reported cases of Ferrier, Bristowe, Mendel, Gowers, Marina, Biancone, Bruns, Raymond, and Cestan the movement is similar to that of a multiple sclerosis. Again it resembles paralysis agitans in the reported cases of Sorga, Touche, Benedict and Eisenlohr. It had a choreiform and convulsive character in the cases of Vigoroux, Greiwe, Henoch, Benedict, Mohr, Henoch-Grawitz, Laignel Lavastine. It is choreiform in the cases reported by Archambault, Bouveret, Halban-Infeld, Kolischer, Bonhœffer, Chapotot, and Ceni, while in a number it is described as athetoid, particularly in those of Leube, Wallenberg, d'Astros-Hawthorne, Van Oordt, Sorgo, Jelliffe, and others.

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*Complete bibliography in paper of Jelliffe, l. c.

It thus becomes evident that a closer scrutiny must be given both to the character of the tremor observed, which fact has been most emphasized by Holmes, and to the exact involvement of the tracts in question.

This appears evident when we note the following divergent opinions. For the sake of clarification we shall consider only three localizations of lesions in this complicated reflex arc (1) Spinal to the red nucleus; *i. e.*, superior cerebellar, tract rubro-spinal-bulbo system; (2) rubro-thalamic and thalamo-rubral; and (3) rubro-cortical, and cortico-rubral:

Thus, one scheme is as follows—:

(1) Spinal=athetoid (Wallenberg).
(2) Rubro-thalamic=Tremor (Touche).
(3) Rubro-Cortical=Chorea (Putnam).

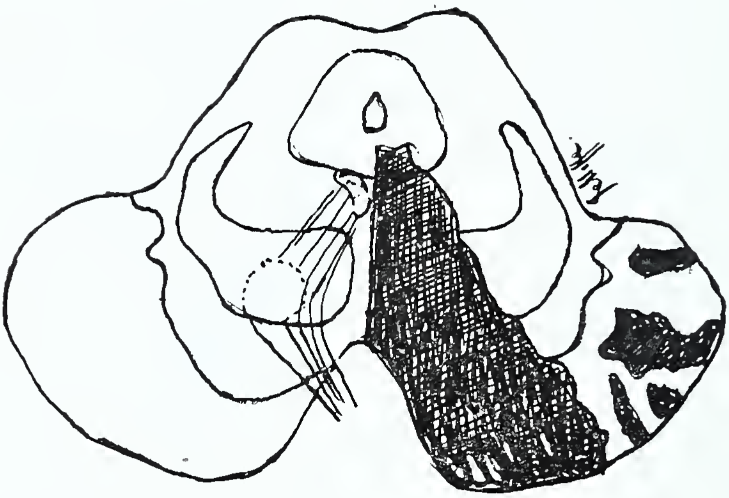

Fig. 5. Cestan's case of Weber syndrome. Location of degeneration in black.

Another arranges them as follows:—

(1) Tegmento-cerebellar=Athetosis.
(2) Rubro-Thalamic=Chorea.
(3) Rubro-Cortical=Tremor.

Holmes in collecting the autopsy findings of 60 cases, believes that the evidence points to athetoid movements when the thalamus is involved; to choreic movements when the mid-brain and ganglia are involved, and to tremor when the lesion is in the mid-brain itself. He does not go into the analysis of the tracts as here outlined.

From my own studies I am disposed to class the athetoid movements as due to an interference with the rubro-thalamic and thalamo-rubral fibres. They usually form a part of the thalamic syndrome of Dejerine and Roussy. (See Jelliffe: Thalamic Syndrome, *Medical Record,* 1909.)

Choreiform and choreo-ataxic movements I am inclined to place in the mid-brain with involvement of the superior cerebellar peduncles; that is when the lesion tends to extend spinally and cerebellarly. Whereas the purely paralysis agitans and multiple sclerosis-like tremors I am inclined to regard as due particularly to the lesions of the rubro-cortical or cortico-rubral fibres, as they sweep through Forel's field, or when the lesion is partly in the nucleus-ruber itself.

Up to the present time, the lesions reported have usually been too extensive to permit close deductions as to the fibre tracts involved—save perhaps in the case of the athetoid movements. Here it would seem that the rubro-thalamic fibres are invariably affected (Hertz). For this reason I am inclined to refrain from taking too positive a position, thus agreeing with both Marburg and Halban-Infeld, that we are not yet in a position to dogmatize.

This brings us back to the consideration of the Benedict syndromes, where, for the most part, the movements are of the paralysis agitans or choreiform type, and where the oculo-motor and pyramidal systems are involved.

The case here reported, however, shows a rather anomalous condition, in that both the oculo-motor and pyramidal symptoms have cleared up, leaving only the tremor and the hemianopsia, agreeing closely with a case reported by Blessing (*St. Petersburg med. Wochenschr.*, 1896).

The latter requires some explanation. It has been found not infrequently with Weber's syndrome. It was present in two of Holmes' cases; Joffroy (*Nouvelle Iconographie de la Salpétrière,* 1898; also *Revue Neurologique,* p. 430, 1900) says it is not infrequent, and refers it possibly to the branches of the posterior communicating which sends branches to the occipital lobe. Brissaud has called attention to the fact that the collateral branches of the posterior cerebral go to the posterior optic tract, and that hemianopsia can result from their involvement. Lesion of the anterior tectal region of the mid-brain can also cause a hemianopsia, and I am inclined to dispose of my case as a lesion of the optic tracts in their ascent to the corpora quadrigemina, and of the rubro-cortical tracts as they sweep out to Forel's field. I shall not exclude, however, a double lesion, implicating the posterior communicating with a lesion of the mid-brain and of the occipital lobes. Furthermore, a basal lesion is not excluded.

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